

The Topical and Systemic Use of Cortisone in Dermatology

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SUMMARY

Part I of this report deals with the topical use of cortisone in a variety of skin diseases. Fifteen patients with chronic discoid lupus erythematosus, four patients with necrobiosis lipoidica diabetorum, four with psoriasis, one with lichen planus and one with granuloma annulare were treated with cortisone ointment. All the patients with chronic discoid lupus erythematosus had some degree of improvement. In two patients with chronic lupus erythematosus, complete clearing of the eruption occurred. In four patients with necrobiosis lipoidica diabetorum remarkable involution resulted. Patients with psoriasis, lichen planus and granuloma annulare were not benefited.

Part II deals with the systemic use of cortisone. Eight patients with severe serum sickness-like penicillin reaction responded dramatically to parenterally administered

cortisone. In two cases of pemphigus vulgaris and one case of Sulzberger-Garbe disease, the disease was kept in remission with cortisone administered intramuscularly as well as orally. Partial improvement resulted in a case of localized myxedema associated with malignant exophthalmus. Two patients with exfoliative dermatitis due to therapy with heavy metals responded dramatically to cortisone. No beneficial effects were noted in patients with chronic urticaria and atopic dermatitis.

The systemic use of ACTH and cortisone in dermatology at present should be confined to patients with known fatal or hopelessly incapacitating diseases and to patients with extreme hypersensitivity reactions which may be protracted or life-endangering, and which can be controlled or cured with a relatively small total dosage of the agents in a short time.

THE introduction of adrenocorticotrophic hormone (ACTH) and cortisone into clinical medicine, and its correlation with Selye's²³ work on the general adaptation syndrome, is no doubt the initiation of a new era in dermatology, if not in all medicine. Therapeutic application of these steroids is still in its infancy, but what perhaps is most momentous is its stimulus to clinical research. The results of experimentation in the basic sciences and in clinical medicine offer great promise of explaining many of the vaguely understood morbid processes of the skin.

The purpose of this presentation is to report the authors' clinical experience in the use of cortisone in the treatment of a variety of dermatoses, after more than a year's study. The first part of this report will deal with the use of cortisone topically, and the second part will be confined to observations on systemic administration. The presentation will be concluded with a synopsis, in table form, of the present-day status of ACTH and cortisone in dermatology.

Eight of the cases reported upon herein were presented at recent meetings of the Los Angeles Dermatological Society.

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Cortisone in Carbowax was supplied by Merck & Co.

TOPICAL APPLICATION OF CORTISONE

The favorable results achieved by ophthalmologists^{22, 29} in the treatment of ocular inflammatory disease with cortisone applied locally suggested that regressive changes in certain dermatoses might follow topical application of the hormone. Due to the difficulty in obtaining cortisone, and because it was felt that more could be learned by a concentrated study on a few appropriate recalcitrant dermatoses (preferably the so-called collagenous diseases), the local use of cortisone was limited primarily to chronic discoid lupus erythematosus. The other dermatoses treated included necrobiosis lipoidica diabetorum, granuloma annulare, psoriasis, and lichen planus.

Originally cortisone was used in the concentration of 3.3 mg. and 5 mg. per gram of Neobase®. Shortly after this study was begun, however, Carbowax® was substituted for the vehicle, and later a concentration of 25 mg. per gram of Carbowax was used.

Chronic Discoid Lupus Erythematosus

Since the original account¹⁵ of the authors' experience in the treatment of chronic discoid lupus erythematosus with topical cortisone was written, the number of cases in the series has been increased; 15 patients with this disease were under treatment at the time of the present report. The duration of therapy ranged from six to 29 weeks. In the patients

studied, the duration of the disease ranged from six months to 17 years, and previous therapy had included the usually employed topical, oral and parenteral medication. Except in three cases (Cases 1, 7 and 15) the group studied were supplied with 25 mg. of cortisone per gram of Carbowax shortly after the investigation was begun, although some at first had been given ointments containing 3.3 mg. and 5 mg. per gram (Table 1). They were instructed to massage the ointment into each of the lesions three to four times daily. In the majority of patients maximal improvement did not occur until treatment with ointment of the higher concentration was begun. Only four patients had pronounced improvement. Except for one small segment of an original patch, one patient (Case 7, Table 1) had complete healing with pigmentation. However, when treatment was discontinued after involution, new small lesions developed in new locations on the face. One patient (Case 1) had complete clearing. In the two other patients (Cases 6 and 12) who had pronounced improvement, the involution was estimated to be over 95 per cent. The rest of the patients had involution ranging from 10 per cent to 75 per cent. In no instance was there untoward reaction either locally or systemically during the period of observation, nor was there any alteration of chemical contents of the blood. Tumid lesions appeared to respond better to topical application of cortisone than did hyperkeratotic lesions. The first change noted after inunction of cortisone was paling, followed by a reduction in the thickness of the lesion. In some patients the eruption took on a glazed appearance. In some instances healing occurred with pigmentation.

Maximal improvement in all the patients occurred within a period of one month after the use of corti-

sone ointment. Except in one patient (Case 7) in whom progressive steady improvement occurred until complete healing, little change was noted in patients continuing to apply cortisone ointment after a period of two months. In patients with flat or hyperkeratotic lesions, there was no more than slight improvement at any time.

REPORT OF A CASE

In the following case (Case 7, Table 1) involution of chronic discoid lupus erythematosus occurred following topical therapy with cortisone.

The patient, a 39-year-old Japanese male, was first observed June 17, 1950. There were erythematous annular and oval-shaped lesions on the face, neck and upper back. Adherent scaling and telangiectasia were noted in some of these areas and there was atrophy in a few patches. A clinical diagnosis of typical chronic discoid lupus erythematosus was made. The eruption had started on the nose in 1945 and later spread to the cheeks, forehead, neck, ears and upper back. In a complete medical and laboratory study carried out in May 1950, no other abnormality was noted.

From June 17, 1950, to Sept. 11, 1950, the patient was given Bistrimate®, crude liver extract, bismuth subsalicylate injections, applications of carbon dioxide ice, and tocopherols; and a 5 per cent para-aminobenzoic acid sun filter cream was prescribed for topical application. There was partial improvement in some of the lesions but most of them progressed. On Sept. 11, the patient was given an ointment containing 3.3 mg. cortisone per gram of Neobase and instructed to massage it into the affected areas three times daily. By Oct. 13 there was about 50 per cent improvement; the lesions were becoming pigmented and were undergoing involution. By Oct. 21 the lesions on the back had healed without pigmentation and those on the cheeks had healed with pigmentation. Lesions below the left eye were about 75 per cent involuted and were partially pigmented, while in a lesion in the left retro-auricular region there was evidence of the beginning of healing for the first time. By Oct. 28 the lesions below the eyes were completely

TABLE 1.—*Chronic Discoid Lupus Erythematosus*

Case No.	Age	Sex	Location of Lesions	Duration	Severity	Concentration Mg. of Cortisone Per Gram of Base	Weeks of Treatment	Degree of Improvement*
1	73	F	Face	10 years	Pronounced	3.3 and 5	6	Cleared
2	35	F	Face	10 years	Moderate	5 and 25	29	Moderate
3	52	F	Face, neck, arms, ears	2 years	Moderate	5 and 25	29	Moderate
4	45	F	Face	8 years	Pronounced	3.3 and 25	25	Moderate
5	41	F	Face	2 years	Mild	5 and 25	18	Slight
6	29	F	Face, scalp	10 months	Pronounced	25	8	Cleared
7	39	M	Face, neck back	5 years	Pronounced	3.3 and 5	17	Pronounced
8	44	F	Face	4 years	Pronounced	25	12	Moderate
9	23	F	Face	3 years	Pronounced	3.3 and 25	12	Moderate
10	30	F	Face	3 years	Moderate	3.3 and 25	12	Moderate
11	32	F	Eyelids	7 years	Moderate	25	10	Moderate
12	42	F	Lips and perioral region	15 years	Pronounced	25	13	Pronounced
13	40	M	Scalp, face	2½ years	Moderate	25	6	Slight
14	33	M	Lips, chin and nose	17 years	Pronounced	25	9	Slight
15	35	F	Cheeks, nose	6 years	Pronounced	10	8	Moderate

* 0-50%, slight; 50%-75%, moderate; 75%-100%, pronounced.

healed and there was only slight erythema remaining in the involved areas in the left retro-auricular region. By Dec. 2 the degree of improvement was 95 per cent.

On Jan. 9 the patient was presented at the meeting of the Los Angeles Dermatological Society to demonstrate the dramatic involution of the eruption. In some of the areas complete healing with pigmentation had occurred while in others pigmentation had decreased and a few remaining spots were atrophic.

The use of the ointment was discontinued at that time. When the patient was next observed, April 14, 1951, all previously treated lesions remained healed except for one residual 8 mm. patch on the left side of the neck. There was slight evidence of fading in residual areas of pigmentation. However, within the ensuing month four new lesions, 4 to 6 mm. in diameter, appeared in other locations on the face.

Necrobiosis Lipoidica Diabeticorum

Four patients with necrobiosis lipoidica diabeticorum confirmed by biopsy were treated with cortisone ointment in the concentration of 25 mg. per gram of base. The patient in whom the disease was the most severe had almost complete involution of lesions after the application of cortisone ointment over a period of eight weeks (the case is reported in detail in following paragraphs). Aside from the dramatic involution of the lesions in this case, the most striking feature was the healing of indolent ulcers within the involved area five days after the institution of treatment. Another patient had 90 per cent improvement after the first seven weeks of application of cortisone ointment. The patient discontinued use of the ointment for a period of three months, and when he was next observed there was no regression of the patch of necrobiosis. A third patient had definite improvement after only two weeks of using the ointment, but unfortunately was lost to further study. In a fourth patient, who at the time of this report had only recently come under the authors' care, there was 75 per cent involution of the lesion after only two weeks of cortisone inunction.

The favorable response noted in all of these patients is significant in view of the notoriously recalcitrant nature of this dermatosis. The method used is the only form of treatment of which the authors are aware that has ever resulted in such rapid response.

REPORT OF A CASE

The patient, a 24-year-old housewife, had diabetes mellitus of 12 years' duration. It had been controlled with insulin during this period. About five years previously a red patch had appeared on the lower part of the left leg and it gradually became larger. About ten months previously the lesion became ulcerated and the patient was given Terramycin®, which had no effect upon the ulcer. The lesion was 8 cm. long and 3 cm. wide, with an L-shaped extension at the lower pole. The borders of the lesion were violaceous; the center was yellowish-orange and contained telangiectatic vessels. At the superior and inferior poles of the lesion there were small superficial ulcers covered with a thick crust. Biopsy confirmed the clinical diagnosis of necrobiosis lipoidica diabeticorum.

During the first week of November 1950, cortisone ointment (3.3 mg. per gram of Neobase) was prescribed, and the patient was instructed to massage it into the lesion four

times daily. The first change noted was dramatic healing of the ulcers by the fifth day. It was then noted that the redness and the yellow-orange color of the lesion were beginning to fade for the first time in five years. On Dec. 8 a more concentrated ointment was substituted (25 mg. of cortisone per gram of Carbowax). During the next two weeks, more pronounced involution was noted. On Jan. 9, 1951, the patient was presented at the monthly meeting of the Los Angeles Dermatological Society. At that time the lesion was smaller in area and there was a reduction of the thickness of the lesion so that when the skin was grasped between the fingers, wrinkling was observed. There were cribriform scars at the site of ulceration and dusky pigmentation of the previously violaceous periphery. The yellow-orange color at the center had changed to light pink. Therapy was discontinued for two months without regression. Cortisone inunction was then resumed and additional involution occurred. When the patient was last observed, there remained only slight tan pigmentation, and atrophic scars at the site of the previous ulcers.

Topical Use of Cortisone in Other Dermatoses

An attempt was made to observe the effects of topical application of cortisone in a small group of cases of unrelated dermatoses. Four patients with psoriasis, one with lichen planus and one with granuloma annulare applied cortisone ointment in the concentration of 25 mg. per gram of Carbowax. The eruption in these patients remained unaffected after therapeutic trial of at least one month.

COMMENT AND SUMMARY OF TOPICAL APPLICATION

At the time of this report, the period of investigation of the use of cortisone topically exceeded seven months. There is better basis for evaluation of the efficacy of topical use of cortisone in the group of dermatoses studied than was available at the time of the authors' previous report.¹⁵ Favorable response ranging from minimal to complete clearing of lesions occurred in chronic discoid lupus erythematosus and necrobiosis lipoidica diabeticorum. No effect was observed in the lesions of psoriasis, lichen planus and granuloma annulare.

It is the authors' belief that if no improvement occurs after eight weeks of application of cortisone ointment, further change is unlikely. From the results of the present study cortisone ointment is obviously not a cure for chronic discoid lupus erythematosus, for healing occurred only at the site of the lesion treated. It could not be expected that topical application of cortisone would prevent the appearance of new lesions. (New eruptions occurred in one case.) The improvement obtained with this form of therapy suggests that it may be used as an adjunct with other methods of treating the disease.

The dramatic effect of topical application of cortisone in all of the patients with necrobiosis lipoidica diabeticorum is most encouraging.

An explanation for the effect of cortisone applied topically is wanting. Whether cortisone thus used acts by affecting the permeability of blood vessel walls, the collagenous fibers directly or its intermediary substance, or by some enzymatic action,

remains to be established. Beneficial effects of locally applied cortisone have been established by ophthalmologists who have reported excellent results in ocular inflammatory conditions after topical instillation²⁹ as well as with subconjunctival injection²² of cortisone. Jones and Meyer¹⁴ experimentally were able to inhibit vascularization of rabbit corneas following alkali burns by previous subconjunctival injection of cortisone. Castor and Baker⁶ demonstrated that regressive changes in the normal skin of the rat can be produced by local application of cortisone in alcoholic solution. They noted thinning of the epidermis, cessation of hair growth, shrinking of sebaceous glands and reduction of dermal thickness by loss of collagen fibers, but no effect on the elastic tissue. They also noted that fibroblasts and other cells of the dermal connective tissue decreased in number. An interesting observation on their part was that after 180 days of therapy, a refractory state developed and hair began to grow.

The fact that, in the present series, improvement of lupus erythematosus progressed up to a certain point and then ceased suggests that a similar refractory state may have developed. Grant, Cornbleet and Grossman⁹ were not able to duplicate the conditions observed by Castor and Baker. Grant and co-workers applied adrenal cortex extract in 25 per cent alcoholic solution to five human subjects for 14 weeks. They observed no evidence that cortical steroids inhibit the growth of skin structure in humans. The suppressive action of cortisone on connective tissue was borne out by Plotz²⁰ and his associates in experimental studies of wound healing. Baker and Whitaker¹ also demonstrated a striking interference in the formation of granulation tissue by direct application of hog adrenal extract dissolved in 25 per cent alcohol solution to cutaneous wounds in rats. However, they observed that adrenal extract prevented the proliferation of fibroblasts and the endothelium of capillaries, for a limited period. Opsahl's¹⁸ work suggested another mechanism of action of adrenal steroids. She noted that adrenal cortical extracts¹⁷ and Compound E¹⁸ inhibited the spreading of intradermally injected india ink with hyaluronidase.

CORTISONE ADMINISTERED SYSTEMICALLY

The widespread use of cortisone in the so-called "collagenous or mesenchymal diseases" led the authors to direct investigation to some of the less frequently reported but appropriate dermatoses in which cortisone might be expected to have an effect. Studies of parenteral use of cortisone were primarily directed toward hypersensitivity states.

Penicillin Reactions

Eight patients with severe reactions to penicillin were treated with cortisone. The patients all had serum sickness-like reactions with fever, arthralgia, angioneurotic edema and extensive migratory urticaria. Patients with lesser degrees of reaction were not included because it was felt that, if they were,

a fair evaluation of the effect of cortisone might not be achieved. All but two of the patients were so severely affected that hospitalization was required. Cortisone was administered intramuscularly in the following manner: 100 mg. each 12 hours for the first 24 hours and then 100 mg. daily until subsidence of the reaction. All subjective and objective symptoms disappeared in two to five days, the average being three days. The response was much more dramatic and rapid than that obtained in similar patients treated with antihistaminics and intravenously administered procaine.

REPORT OF A CASE

A 37-year-old male received penicillin injections Dec. 22, 23 and 24, 1950, because of injuries received in an automobile accident. On Jan. 2, 1951, the patient noted severe itching of the scrotum and inguinal regions, and the following day there was pronounced edema and erythema of the scrotum as well as erythema, scaling and eczematization of the inguinal and perianal areas. There was generalized urticaria with angioneurotic edema of the face and hands, and pronounced swelling and tenderness of the wrists and elbows. The patient complained of pain in the joints and the temperature rose from 100° F. to 103° F. He was hospitalized and received 100 mg. of cortisone twice daily for the first 48 hours and a total of 100 mg. during the succeeding 24 hours. Within 24 hours after therapy was started the temperature was normal and the arthralgia had abated. Most of the urticarial lesions had disappeared by the end of 48 hours but angioneurotic edema to a lesser degree was still evident. At the end of 72 hours the patient was completely free of all previous subjective and objective symptoms.

Pemphigus Vulgaris

Two patients with pemphigus vulgaris were treated. One, a 70-year-old man with severe bullous pemphigus of nine months' duration, received 100 mg. of cortisone intramuscularly daily for ten days. Rapid involution of all lesions occurred. Cortisone to be taken orally was then prescribed, in doses of 75 mg. daily, decreasing to 50 mg. per day. When cortisone dosage was further reduced, a few scattered blebs and bullae appeared; when it was increased to 50 mg. daily again the patient became and remained symptom-free.

The other patient (who was presented at a meeting of the Los Angeles Dermatological Society after the first remission) had been under observation for 12 months at the time of this report. Because of unusual features, the case of this patient is presented in detail.

REPORT OF A CASE

A 50-year-old white male had pemphigus of two years' duration. There were profuse erosions and clear blebs of the mucous membranes of the tongue, cheeks, pharynx, and of the vermillion borders of the lips, as well as vegetative lesions of the perianal and inguinal regions. Pemphigus vegetans was confirmed by biopsy, and by several dermatologists throughout the country. Past treatment had included aureomycin, bacitracin, acetarsone, sodium naphthyl, x-ray therapy, transfusions and sulfonamides. There had been a single partial remission for two weeks following acetarsone therapy but relapse occurred despite an

increase in dosage. Therapy with cortisone acetate was started April 12, 1950. At that time there were thick vegetative lesions in the anogenital region, profuse erosions of the oral cavity and crusted lesions of the lips. Because of pain in the mouth, eating was difficult and the patient had lost 30 pounds in weight in six months. On the basis of reports that cortisone inhibits granulation tissue, it was thought that the administration of this steroid might have some effect upon the vegetating lesions of pemphigus. The dosage schedule was as follows: 100 mg. daily intramuscularly for four days; 75 mg. daily for four days; 50 mg. for four days; and 25 mg. every second day for three doses. From April 12 to May 7 the patient received a total of 975 mg. of cortisone acetate. The soreness of the mouth disappeared in four days, the vegetative lesions healed in eight days and the mouth was free of lesions in 14 days. On May 18, two weeks after discontinuance of treatment, a new crust appeared on the left side of the lower lip. By June 5 the entire lower lip was crusted and a few erosions began appearing in the mouth. On June 22, granulations of the inguinal region began to recur, and there were additional oral lesions. Cortisone therapy was reinstituted and from July 8 to August 1 the patient received 1,125 mg. Again the eruptions subsided rapidly. From Aug. 1 to the time of discontinuance of therapy on Jan. 8, 1951, the patient was given maintenance doses which were gradually reduced to only 50 mg. weekly. For nine months up to the time of this report (four months after discontinuance of therapy) the patient had had only occasional evanescent erosions in the mouth. There was no recurrence of vegetative lesions in the groin, and when last observed the patient was in excellent health and doing a full day's work.

Chronic Exudative Discoid and Lichenoid Dermatitis (Sulzberger-Garbe)

The case of one patient with this syndrome, who was treated with cortisone and observed over a period of eight months, is presented in detail:

REPORT OF A CASE

A 66-year-old white male, first observed Aug. 14, 1950, had intensely pruritic and excoriated, generalized, maculopapular and patchy, erythematous, scaly, exudative dermatosis. For two years he had been unable to work and had been under dermatological therapy constantly, including hospitalization at the Los Angeles County General Hospital on two occasions in 1949 (Sept. 28 to Nov. 21, and Nov. 30 to Dec. 15). During each hospital stay the symptoms cleared with bland therapy, but recurred immediately after discharge. Sodium arsenate, penicillin, x-ray therapy, Benadryl®, starch baths, permanganate baths, lotions and ointments, phenobarbital, Vioform® and Fowler's solution had been ineffective in the past. Result of a biopsy at the Los Angeles County General Hospital on Sept. 30, 1949, was reported consistent with the diagnosis of Sulzberger-Garbe disease.

From Aug. 24, 1950, to Dec. 20, 1950, cortisone was given intramuscularly: 100 mg. daily for four days, then 75 mg. daily for six days, and 50 mg. every second day for three doses. By Sept. 8, there was about 50 per cent improvement subjectively and objectively. Between Sept. 9 and Nov. 1, 50 mg. of cortisone was given intramuscularly every other day. From Nov. 1 to Dec. 20, 50 mg. was administered once weekly. Steady progressive improvement continued until Dec. 1. Itching during the day was completely eliminated and the patient was able to resume gainful employment for the first time in two years. On Dec. 20 there was partial relapse, subjectively and objectively. The dosage of corti-

sone was then increased as follows: 75 mg. intramuscularly on Dec. 20, 22 and 27; 75 mg. orally per day, from Dec. 27, 1950, to Jan. 31, 1951. From Feb. 1 to March 6 the dose was 50 mg. daily, and from March 7 to April 18 it was 50 mg. every other day. Since then the patient has taken 50 mg. orally once weekly, without relapse.

The second course of cortisone therapy resulted in even more striking improvement than was observed initially. At the time of report, the skin was practically free of all lesions, with only occasional itching during the night, and the patient was able to continue working. At no time was there any untoward effect clinically, and there were no changes in results of laboratory tests except for a reduction in the proportion of eosinophils from 22 per cent to 1 per cent.

Localized Myxedema Associated with Malignant Exophthalmus

The authors observed a 56-year-old man with malignant exophthalmus and extensive pretibial myxedema that appeared after radioactive iodine therapy for hyperthyroidism. The exophthalmus had progressed to such a degree that orbital decompression had been recommended. Cortisone was given and within two weeks—a total of 600 mg. of the hormone was given during the period—there was considerable regression of both the exophthalmus and the pretibial myxedema. Several weeks later another 900 mg. of cortisone in divided doses was administered, and there was 75 per cent regression of the exophthalmus and almost complete involution of the localized myxedema. Nine months later, mild relapse was noted but it was insufficient for the patient to desire additional therapy.

Exfoliative Dermatitis

Two patients with generalized erythroderma following gold therapy for arthritis were treated with cortisone. The first patient, a male 40 years of age, had seborrheic-like dermatitis of the scalp and all the intertriginous areas which rapidly spread over the entire body. There was edema and weeping of all the flexural surfaces. A course of British anti-lewisite was administered with no effect upon the dermatitis. Two weeks later cortisone was given, 100 mg. intramuscularly daily for six days, with dramatic involution; then 50 mg. intramuscularly daily for five days. One week later there was mild recurrence of the seborrheic-like dermatitis, but it was controlled with oral administration of 50 mg. of cortisone daily for three weeks. In the other patient, a 52-year-old woman, similar extensive seborrheic-like dermatitis developed soon after gold therapy and it gradually extended to involve the entire body with erythroderma. There were exudative lesions of the flexural surfaces. A course of British anti-lewisite (BAL) initially induced considerable improvement, but relapse soon followed. Another course of BAL was ineffective. Several weeks later cortisone was administered intramuscularly, 100 mg. daily for four days, 75 mg. for four days, and 50 mg. for six days, for a total of 1,000 mg. Involution of the dermatitis was prompt and complete.

However, two weeks later there was partial relapse. The patient was then given cortisone 50 mg. intramuscularly daily for two weeks; then 50 mg. every other day for two weeks. She remained well thereafter.

Atopic Dermatitis

Three male patients with long-standing atopic dermatitis so severe as to make hospitalization necessary, did not have satisfactory response to cortisone given in the dosage schedule advocated for rheumatoid arthritis. In one patient who had early favorable response to the hormone, increased dosage was required to maintain the initial improvement. When cortisone was discontinued there was prompt relapse and the disease then was more severe than it had been before the hormone was given.

Negative Results

Three patients with chronic urticaria of long duration and of unknown cause had no response to cortisone acetate administered intramuscularly.

ADRENOCORTICOTROPIC HORMONE (ACTH)

The authors' experience with ACTH has been too recent and too limited to warrant a detailed report of observations. The hormone was used in treating postpartum toxic dermatitis, autosensitization dermatitis, generalized subacute exudative neurodermatitis and severe bullous erythema multiforme-like penicillin reaction. In the patients treated for these conditions, the lesions cleared following use of ACTH in doses comparable to those advocated for rheumatoid arthritis. The results were similar to those obtained with cortisone. It was the authors' impression that the response to ACTH was perhaps even more rapid than that which occurred when cortisone was given. However, that opinion is based on observation of only a very small number of patients treated with ACTH.

The authors believe that ACTH may be more rationally employed to obtain an initial rapid response as reported by Irons¹³ and co-workers, and that cortisone might be used subsequently in maintenance doses, with the dosage gradually reduced to complete discontinuance.

COMMENT AND SUMMARY ON USE OF CORTISONE SYSTEMICALLY

The response of eight patients with severe serum sickness-like penicillin reactions treated with cortisone was dramatic in that the reactions were terminated in two to five days. Fever and subjective complaints usually subsided within 24 hours. Dramatic improvement and healing were also observed in patients with exfoliative dermatitis.

Maintenance of remission in two patients with pemphigus vulgaris compares with the experience of others.⁵ To date this steroid offers only remission for this usually lethal disease. Whether ACTH or cortisone will prove to be curative is questionable,

and many years of observation will be required to come to any definite conclusion. Results were favorable in the treatment and observation of a patient with Sulzberger-Garbe disease over a period of eight months, but again it appears that only remission will be possible.

Hench's¹⁰ classic comment that "cortisone appears to have little or no effect on the irritant but seems to provide the susceptible tissue with a shield-like buffer against the irritant" apparently still holds true. However, cortisone is more than just a hormonal agent capable of causing remissions in some previously recalcitrant or fatal skin diseases. At present it is, in the authors' view, the definitive drug of choice in the treatment of certain hypersensitivity states: (1) Dermatitis medicamentosa, such as severe reactions to penicillin, and exfoliative dermatitis due to drugs (including heavy metals), and (2) autosensitization dermatitis with severe generalized cutaneous involvement. In such conditions, the hormone offers clinical cure. It is true that such conditions may be self-limited, but cortisone so shortens the course that diseases which might be prolonged or even life-endangering are relatively innocuous.

In short, it appears that cortisone and ACTH are effective in two main groups of dermatoses. First, in the so-called collagenous diseases, and secondly in dermatoses characterized by a sensitivity state. In the collagenous or mesenchymal diseases, the effects of these hormonal agents are not curative, but use of them has induced remissions for varying periods. In the hypersensitivity states they are not truly curative, but they do act more definitely in that they shorten and reduce the intensity and duration of the pathologic manifestations.

Probably the greatest significance of cortisone and ACTH in dermatology, and perhaps in the whole field of medicine, lies in the stimulus to basic research and the promise for a physiopathologic explanation for some of the little understood but grave disease entities. The implication and correlation with Selye's²³ work is very interesting. ACTH and cortisone apparently influence the adaptive processes of the patient whether the original sensitizing agent be truly allergic or toxic.

Enthusiasm for these hormones should be tempered with caution. Reports of many varieties of serious reactions have already appeared. It is the authors' opinion that systemic administration over long periods or in large doses is justified only for experimental purposes by experienced groups. As regards diseases of the skin, cortisone and ACTH should be used clinically only for patients with known fatal or hopelessly incapacitating dermatoses, and for patients with extreme hypersensitivity reactions which may be protracted or life-endangering. In the latter group there is justification for the use of these steroids if the morbid process can be controlled or cured in a short period of time with a relatively small total dosage. The authors are op-

posed to the administration of cortisone or ACTH in large and prolonged dosage to patients who have chronic dermatosis of a kind known to recur when the therapy is discontinued.

TABLE 2.—*Summary of Reported Results with Cortisone and ACTH in Treatment of Skin Diseases*

UNIFORMLY BENEFICIAL EFFECTS (GENERALLY DRAMATIC)

1. Drug eruptions
 - Severe penicillin reaction^{2, 12}
 - Exfoliative dermatitis²
2. Severe auto-sensitization eruption
3. Toxic dermatitis

TRANSITORY BENEFICIAL EFFECTS

1. Lymphosarcoma¹⁹
2. Hodgkin's disease¹⁹
3. Other lymphomas¹⁹

REMISSIONS INDUCED—ULTIMATE CURE QUESTIONABLE
(USUALLY REQUIRE MAINTENANCE DOSE)

1. Acute disseminated lupus erythematosus^{4, 8, 13, 26, 27}
2. Dermatomyositis^{8, 27}
3. Psoriatic erythroderma²⁷
4. Psoriasis with arthropathy¹³
5. Psoriasis vulgaris^{13, 16, 27}
6. Scleroderma^{8, 11, 24}
7. Scleroderma (ACTH only)¹³
8. Periarteritis nodosa^{13, 25}
9. Atopic dermatitis
10. Pemphigus vulgaris^{5, 27}
11. Long-standing erythroderma¹³
12. Pemphigoid eruptions⁵

NO EFFECT IN:

1. Sarcoidosis²⁷
2. Mycosis fungoides²⁸
3. Herpes simplex²⁷
4. Varicella²⁷
5. Herpes zoster²⁷
6. Moniliasis²⁷
7. Epidermolysis bullosa⁵
8. Melanocarcinoma¹⁹

QUESTIONABLE EFFECTS IN:

1. Chronic discoid lupus erythematosus¹³
2. Advanced scleroderma
- *3. Psoriasis vulgaris
- *4. Atopic dermatitis

UNFAVORABLE EFFECTS MAY OCCUR IN PATIENTS WITH:

1. Acne vulgaris
2. Hirsutism
3. Periarteritis nodosa^{13, 25} (marked occlusive arterial tendency during healing reported by Shick and Irons)
4. Scleroderma²⁴ (thrombotic ischemic infarctions of kidney—Sharnoff)
5. Prepsychotic states
6. Hypertension²⁶
7. Bacteremia and septicemia⁷
8. Tuberculosis
9. Renal insufficiency
10. Congestive heart failure²⁶
11. Diabetes mellitus

*Note: It is the authors' opinion that relapse following discontinuance of the hormone may be more severe than the original disease.

REVIEW OF LITERATURE ON SYSTEMIC USE OF ACTH AND CORTISONE IN DERMATOLOGY

It is apparent that definite conclusions cannot be drawn from reports in the literature on the use of ACTH and cortisone in dermatologic conditions because of the limited time that these agents have been used. Except for reports on the use of these steroids in the collagenous diseases the published information is meager. In some instances there is a divergence of opinion regarding the efficacy of ACTH over cortisone.¹³

In Table 2 an attempt is made to correlate data from the literature with the authors' observations and information received in personal communications from other physicians.

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